Office Action Summary	Application No.	Applicant(s)
	10/582,893	KLAVENESS ET AL.
	Examiner	Art Unit
	Leah Schlientz	1618

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-8 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-8 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)	
1) ☐ Notice of References Cited (PTO-892)	4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) ☐ Notice of Informal Patent Application
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.	6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/09/2010 has been entered.

Acknowledgement of Receipt

Applicant's Response, filed 11/09/2010, in reply to the Office Action mailed 6/08/2010, is acknowledged and has been entered. Claim 1 has been amended. Claims 1, 6-8 and 11 are pending and are examined herein on the merits for patentability.

Response to Arguments

Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection set forth in view of claim amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 6-8 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ke *et al.* (*Cancer Res.*, 63, p. 7870-7875, November 15, 2003) in view of Cuartero-Plaza *et al.* (*Clinical Cancer Research*, 1996, 2, p. 13-20).

Ke discloses near-infrared optical imaging of epidermal growth factor receptor in breast cancer xenografts. The specificity of a novel epidermal growth factor (EGF)-Cy5.5 fluorescent optical probe in the detection of EGF receptor (EGFr) was assessed using continuous-wave fluorescence imaging accomplished via an intensified charge-coupled device (CCD) camera. *In vivo* imaging was performed on mice with s.c. MDA-MB-468 and MDA-MB-435 tumors. Images were obtained every 6 s for 20 min after i.v. injection of each agent and every 24 h after injection for up to 192 h. In MDA-MB-468

tumors, our data suggest that **EGF-Cy5.5** may be used as a specific NIR contrast agent for noninvasive imaging of EGFr expression and monitoring of responses to molecularly targeted therapy (abstract). EGFr is a transmembrane glycoprotein with an intracellular tyrosine kinase domain. EGFr and its ligands, including EGF, are frequently overexpressed in a variety of solid tumors, including **cancers** of the brain, breast, colon, head and neck, **lung**, ovary, and pancreas. Overexpression of EGFr is associated with increased metastatic potential and poor prognosis. NIR images and intensity-time curves from dynamic NIR imaging might be used to characterize the presence of EGFr and to monitor therapies directed at EGFr (page 7870, right column). Recombinant human EGF was used (Mr 6,215) (i.e. a polypeptide), and conjugated to Cy5.5 (page 7870, right column).

Accordingly, Ke teaches near-infrared optical imaging of epidermal growth factor receptor in breast cancer xenografts using EGF-Cy5.5, but does not specifically demonstrate imaging of lung cancer.

Cuartero-Plaza discloses that overexpression of epidermal growth factor receptor (EGFr) in squamous carcinomas has been demonstrated extensively. Preliminary clinical studies have shown that radiolabeled anti-EGFr monoclonal antibodies can localize to these tumors. The aims of this study were to determine the tolerance, pharmacokinetics, and radiolocalization properties of 131I-labeled EGF in patients (n = 9) with advanced squamous lung cancer. Patients' vital signs and symptoms were monitored regularly for 3 days. Daily scintigrams and biological samples for pharmacokinetic analysis were obtained for 3-4 days. 99mTc-labeled human serum

albumin was administered to patients with positive tumor scans. Six patients had positive tumor scans, and five of them had received >/=1.0 mg EGF. In all of these cases, tumors were visualized the same day of the infusion, although best tumor-background contrast was obtained at 50-74 h. There were no false-positive images. Whole-body radioactivity retention rose significantly with increasing EGF doses; most labeled EGF was eliminated by urinary excretion. Tumor normal tissue uptake ratios increased during the course of the study. All patients presented self-limited, dose-related gastrointestinal adverse effects. In conclusion, recombinant 131I-labeled EGF administered i.v. can localize to squamous lung cancer efficiently, can be administered safely to patients, and has more advantageous pharmacokinetic properties than monoclonal antibodies. Further studies are warranted to determine more accurately the potential of EGF and EGF-related peptides in the imaging and/or therapy of EGFr-overexpressing human cancers (abstract).

Cuartero-Plaza discloses ^{131}I-labeled EGF, rather than cyanine-labeled EGF.

It would have been obvious to one of ordinary skill in the art at the time of the invention to perform optical imaging of lung cancer associated with overexpression of EGFr upon administration of EGF-Cy5.5 because Ke shows that EGF-Cy5.5 is used as a specific NIR contrast agent for noninvasive imaging of EGFr expression, such as in optical imaging of breast cancer xenografts. One would have been motivated to do so because Ke teaches that EGFr overexpression is known in a variety of solid tumors, including cancers of both breast and lung. One would have had a reasonable

expectation of success in doing so because Cuartero-Plaza shows that labeled EGF localizes squamous lung cancer efficiently for imaging (abstract).

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is (571)272-9928. The examiner can normally be reached on Monday-Wednesday 9 AM-5 PM and telework Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LHS/
/MICHAEL G. HARTLEY/
Supervisory Patent Examiner, Art Unit 1618